OnG7: A Metal–Organic Framework for Potential Chemotherapeutic Delivery in Breast Cancer Treatment

Darragh McHugh [a], Sha Li[b], Róisín M. Dwyer [b] and Constantina Papatriantafyllopoulou [a]

[a] School of Biological and Chemical Sciences, College of Science and Engineering, University of Galway, H91 TK33 Galway, Ireland.

[b] School of Medicine, Lambe Institute for Translational Research, University of Galway, Galway, Ireland

Background: While cancer treatments continue to evolve, metastatic and surgery-resistant cancers—such as triple-negative breast cancer (TNBC)—remain among the most challenging to treat, with limited therapeutic options and poor prognoses. Enhancing drug bioavailability in tumours while minimising off-target toxicity is critical for improving treatment outcomes. In recent years, metal–organic frameworks (MOFs) have emerged as promising nanocarriers due to their high drug-loading capacity, biocompatibility, and tuneable properties.

Methods: OnG7 was synthesised via solvothermal synthesis, with structural characterisation performed using SCXRD, SEM, TEM, and gas sorption analysis. Particle size and stability were evaluated using DLS and zeta potential measurements. Drug loading was performed via impregnation techniques, and release profiles were analysed in PBS at varying pH levels using UV-Vis spectroscopy. Cellular uptake was assessed by flow cytometry and cytotoxicity was evaluated in MDA-MB-231 and BT-20 TNBC cell lines via AlamarBlue assays, while drug uptake and internalisation were investigated using confocal microscopy in 2D cell culture and 3D Multicellular Breast Cancer Models.

Results: Here, we present OnG7 (where OnG stands for Ollscoil na Gaillimhe (University of Galway)), a novel porous MOF designed for drug encapsulation and controlled release. Constructed from a zinc-oxo cluster and an elongated multitopic carboxylate linker, OnG7 exhibits a mesoporous architecture with a surface area of approximately 5000 m^2/g and pore size of 2.2 nm. Dynamic light scattering and zeta potential analysis revealed nanoparticle sizes of 310.4 ± 18 nm with a surface charge of -12 ± 0.1 mV under physiological conditions.

Following the high loading of doxorubicin (49.6 ± 1.2 wt %) and paclitaxel (36.1 ± 1.5 wt %), OnG7 formulations were assessed for colloidal stability and biocompatibility. In vitro studies on two TNBC cell lines demonstrated efficient cellular internalisation, low cytotoxicity in drug-free formulations, and sustained drug release. Notably, investigations using a 3D multicellular breast cancer model revealed DOX@OnG7 retention within the hypoxic core.

Conclusions: These findings support OnG7's potential as a drug delivery platform and further its clinical translation. Future studies should explore surface functionalisation with targeting moieties for cancer cells to enhance therapeutic precision, followed by in vivo evaluation.

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